

1 REMARKS

2 Status of the Claims

3 Claims 34-53 are pending in the present application, Claims 1-33 having been canceled as  
4 being directed to a non-elected invention, and new Claims 52 and 53 having been added in the  
5 present amendment. Claims 34-38, 40 and 41 have been amended to more clearly define the  
6 invention.

7 Amendment to the Specification

8 The amendment to the specification does not add any new matter, and eliminates the  
9 possibility that U.S. Patent No. 6,249,341 could be incorrectly perceived as prior art. The '341 patent  
10 was filed on January 24, 2000, and issued on June 19, 2001. The present application has a priority  
11 date of February 21, 2001, therefore the '341 patent cannot be prior art. The '341 patent discloses an  
12 imaging system that can be used to image objects in flow. The '341 patent describes that an  
13 exemplary utilization of the novel flow imaging system of the '341 patent is to analyze biological  
14 cells labeled using single color FISH probes. The single color FISH probes themselves are prior art,  
15 thus FIGURE 2A of the present application is properly labeled *PRIOR ART*. It should be understood  
16 that the image portion of FIGURE 2A can be considered to be prior art, so long as the image is  
17 collected using a prior art imaging system, and not the flow imaging system that was the subject of  
18 the '341 patent. The amendment simply clarifies that it is the single color FISH probes which are  
19 prior art, and not the '341 one patent itself. The amendment to the specification further corrects an  
20 error in the identification of elements in FIGURE 2A, to ensure that the reference numbers in the  
21 Figure correspond to the reference numbers in the text.

22 Rejections of Claims 34-51 under 35 U.S.C. § 112

23 The Examiner has rejected Claims 34-51 under 35 U.S.C. § 112, second paragraph, as being  
24 indefinite for failing to particularly point out and distinctly claim the subject matter which applicant  
25 regards as the invention. In particular, the Examiner asserts the term "feature" is indefinite, because  
26 the claims recite that a labeled probe can be bound to a feature, and the Examiner considers color to  
27 be a feature to which a labeled probe cannot be bound. The Examiner further asserts that the terms  
28 "object," "associated," and "sufficient" are indefinite, as well as the phrases "at least a portion of the  
29 feature" and "spectral composition of light." Applications respectfully disagree for the following  
30 reasons.

1           The Indefiniteness of the Term "Feature" in Claims 34 and 42

2           The Examiner has asserted that the term "feature" is indefinite because the Examiner  
3 considers a color of an object to be a feature, and logically one cannot bind a labeled probe to a color.  
4 However, applicants have never asserted that a labeled probe should bind to a color of an object, nor  
5 is it apparent that one of ordinary skill in the art would have considered a feature of an object to  
6 which a probe can be bound to be a color, given the context of the disclosure in the present invention.  
7 The specification uses the terms cellular feature and cellular component interchangeably. For  
8 example, the *Field of the Invention* section states that the present invention "...generally relates to a  
9 method and apparatus employed to probe and simultaneously analyze a plurality of cellular features,  
10 and more specifically, employs biomolecular probes labeled with different fluorescent markers in a  
11 multiplex color encoding scheme in which each probe produces a unique combination of colors (page  
12 1, lines 8-12)." The *Background of the Invention* section contrasts the present invention's multiplex  
13 color probe encoding scheme with prior art encoding schemes used for "...the probing of various  
14 cellular components (page 1, line 14)." The *Background of the Invention* section goes on to describe in  
15 detail various different cellular components to which probes can be bound. Indeed, the *Background of the*  
16 *Invention* section provides a detailed description of the use of Fluorescence *In-Situ* Hybridization (FISH)  
17 probes, specifically using the term "feature" to describe how different FISH probes can be bound to  
18 different features of a cell. It does not appear reasonable to conclude that one of ordinary skill in the  
19 art would not understand that the singly colored FISH probes are bound to physical features of a  
20 biological cell, given that the use of singly colored FISH probes is well understood in the art.

21           Clearly, one of ordinary skill in the art would have understood that the term feature as used in the  
22 specification and claims was synonymous with the term component. The term cellular feature was not  
23 used in the claim language, because while an exemplary use of the present invention is the analysis of  
24 biological cells, the same principle could be used to probe non-biological objects which also exhibit  
25 features or components to which a probe could be bound. This concept of expanding the scope of the  
26 invention to objects other than biological cells is explicitly stated in the *Summary the Invention*,  
27 which notes that: "The present invention is directed to a method and apparatus for the probing and  
28 subsequent simultaneous analysis of a multitude of features in cells, biological matter and other  
29 objects (page 6, lines 17-19)."  
30

1 Applicants note that MPEP 2173.05 specifically states that the examiner's focus during  
2 examination of claims for compliance with the requirement for definiteness of 35 U.S.C. § 112,  
3 second paragraph, is whether the claim *meets the threshold requirements of clarity and precision, not*  
4 *whether more suitable language or modes of expression are available* (emphasis added).  
5 MPEP 2173.05 goes on to note that *some latitude in the manner of expression and the aptness of*  
6 *terms should be permitted* even though the claim language is not as precise as the examiner might  
7 desire (emphasis added). In particular, MPEP 2173.05 indicates that the essential inquiry is whether  
8 the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and  
9 particularity. Definiteness of claim language must be analyzed, not in a vacuum, but in light of: (A)  
10 The content of the particular application disclosure; (B) The teachings of the prior art; and (C) The  
11 claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent  
12 art at the time the invention was made.

13 The specification as filed clearly uses the terms feature and components synonymously. An  
14 example is provided in the *Background of the Invention* describing how single color FISH probes  
15 bind to "feature" of a cell. Practitioners of ordinary skill in the art would be readily familiar with  
16 using FISH probes to selectively bind to various different cellular components, such as cell nuclei  
17 and cellular proteins. It appears reasonable to conclude that one of ordinary skill in the art would  
18 readily understand the use of the term "feature" in the claim language. Clearly, practitioners of the  
19 art understand that probes can be bound to various physical components or features of an object such  
20 as a cell, and that probes are not bound to a color. Clearly, some objects *do* have features (i.e., for a  
21 cell, such features include the nucleus, cytoplasm, or specific proteins) to which a labeled probe can  
22 be bound. The fact that the Examiner can consider a color to be a feature does not change the fact  
23 that labeled probes can be bound to features such as proteins, nuclei and cytoplasm. It appears  
24 illogical to conclude that one of ordinary skill in the art would not understand the meaning of the  
25 term feature as used in the specification and claims of the present application. The appropriate test  
26 for indefiniteness is not whether *some* person could theoretically be confused by a term in a claim,  
27 but rather whether one of ordinary skill in the art would be confused by that term.

28 Significantly, the Examiner had no trouble understanding that the meaning of the term feature  
29 was intended to be synonymous with the term component, and where the object is a cell, such  
30 components would include the nucleus, cytoplasm, or specific proteins within a cell. Therefore,

1 given that the term was sufficiently clear for the Examiner to understand, that some latitude should be  
2 given to applicants' choice of language, and that there is no basis to conclude that one of ordinary  
3 skill in the art would not understand the meaning of the term feature, the rejection of the claims under  
4 35 U.S.C. § 112, second paragraph, as being indefinite for the use of the term "feature," should be  
5 withdrawn.

6 The Indefiniteness of "At Least a Portion of the Feature" in Claims 34, 40, 42 and 46

7 With respect to the rejection of Claims 34, 40, 42 and 46, the Examiner has indicated that the  
8 term "at least a portion of the feature" is a relative term, which renders the claim indefinite. The  
9 Examiner asserts that at least a portion is not defined by the claim or the specification, and no  
10 standard for ascertaining the requisite degree has been provided, thus one of ordinary skill in the art  
11 would not reasonably be apprised of the scope of the invention. Applicants respectfully disagree.

12 The purpose of the inclusion of the term at least a portion of the feature was intended to  
13 recognize that some features (i.e., some components of a cell or other object) can accommodate more  
14 than one probe. This is explicitly described in the specification and drawings as filed. For example,  
15 FIGURE 2D schematically illustrates Features 1-3, each of which include three distinct binding sites  
16 upon which a probe can be bound (i.e., three different probes can be bound to each feature in  
17 FIGURE 2D). Clearly, binding a probe to at least a portion of a feature refers to binding a probe to at  
18 least one binding site on a feature including a plurality of binding sites. The specification and  
19 drawings as filed specifically disclose features including a plurality of binding sites. For example,  
20 the specification clearly describes the single protein molecule will exhibit a plurality of different  
21 binding sites (at different domains or subunits of a given protein (see page 9, line 28, to page 10,  
22 line 3).

23 There appears to be no indefiniteness issue here, nor would it appear that the specification  
24 ought to have included more detail. Logically, if the feature includes multiple binding sites, probes  
25 can be bound to a least one of those binding sites, or all of those binding sites. No further  
26 explanation appears to be warranted. Logically, the number of possible binding sites associated with  
27 a particular feature is a function of the relative size of the feature, and at the relative size of each  
28 probe to be bound to the feature. Relatively larger features and relatively smaller probes would  
29 logically result in relatively more binding sites than could be accommodated by relatively smaller  
30 features and relatively larger probes. It would not appear that this concept needs to be explained in

1 detail, beyond indicating that different features can accommodate different numbers of probes, a  
2 concept which is clearly encompassed in the specifications and drawings as filed. Accordingly, the  
3 rejection of the claims under 35 U.S.C. § 112, second paragraph, as being indefinite for the use of the  
4 term "at least a portion of the feature," should be withdrawn.

5 The Indefiniteness of the Simultaneous Use of "Object" and "Feature" in Claims 34 and 42

6 The Examiner further asserts that the terms "feature" and "object" in Claim 34 and 42 are  
7 indefinite, because it is unclear how each term should be interpreted, specifically because the  
8 specification on pages 6 and 7 uses the terms feature and object interchangeably.

9 The specification makes it clear that a particularly preferred implementation of the present  
10 invention involves objects which are biological cells including a plurality of different cellular features  
11 (i.e., cellular components). The claims employed the term object in place of cell, specifically because  
12 the multiplex encoding scheme at the present invention can be used in conjunction with analyzing  
13 objects that are not biological cells, wherever probes can be bound to an object. Logically, some  
14 objects may include a plurality of different features, just as biological cells include a plurality of  
15 different features. Other objects may not include a plurality of distinct separate features. For  
16 example, a micro-sphere or bead represents an object having a relatively uniform surface that does  
17 not include a plurality of different distinguishable features to which a probe can be bound. Indeed,  
18 one of ordinary skill would refer to such a uniform object as being *featureless*. However, probes can  
19 still be bound to the surface of such featureless objects. Thus, the multiplex probe encoding  
20 technique of the present invention could theoretically be used to bind probes to an object that does  
21 not include distinguishable features, by using different signaling elements attached to a binding  
22 element selected to bind to the bead or micro-sphere. This represents a concept that has been briefly  
23 disclosed, but not claimed, in the claim set currently being examined.

24 Clearly, while it is logically possible for an object to exist which does not include any  
25 distinguishing features (objects such as micro-spheres), the object recited in Claims 34 and 42 *must*  
26 include at least one feature. There is no ambiguity between the object and feature recited in  
27 Claims 34 and 42. Accordingly, the rejection of Claim 34 and Claim 42 under 35 U.S.C. § 112,  
28 second paragraph, as being indefinite for the simultaneous use of the terms "object" and "feature,"  
29 should be withdrawn.

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1           The Indefiniteness of the Term "Associated with the Object" in Claims 34, 42, 43 and 47

2           The Examiner further asserts that the term "associated with the object" as employed in  
3 Claim 34, step (b), is ambiguous (the phrase is similarly employed in Claims 42, 43 and 47).  
4 Respectfully, applicants do not understand Examiner's position. As would be recognized by someone  
5 of ordinary skill in the art, one use of labeled probes is to enable a population of cells or other objects  
6 to be analyzed. Some members of that population may include specific features to which probes will  
7 be bound, whereas other members of that population may not express or include a specific feature to  
8 which a specific probe will be bound. Analyzing that population will enable a determination to be  
9 made as to whether a specific object or cell in that population includes a specific feature. The method  
10 recited in Claim 34 can be used to determine whether a particular feature is present in or on a  
11 particular object. The term associated with has been employed because features of objects can be  
12 internal (i.e., a nucleus or other internal component) or external (i.e., a surface protein). Logically,  
13 both internal and external features are encompassed by the term "associated with an object" (clearly,  
14 both a cell nucleus and a surface protein are associated with a cell). The term "on the object" would  
15 be insufficient because some features may not be on the surface of an object, but may be contained  
16 within an object, such as a nucleus. The term "in the object" would also be insufficient because some  
17 features may not be encompassed within an object, such as surface proteins present on the outer  
18 surface of a cell. While applicants could have used the term "part of the object," MPEP 2173.05  
19 clearly articulates the concept of allowing an applicant some latitude in the manner of expression and  
20 the aptness of terms, particularly if there is no evidence that the terms employed would not have been  
21 understood by one of ordinary skill in the art. Accordingly, the rejection of Claims 34, 42, 43 and 47  
22 under 35 U.S.C. § 112, second paragraph, as being indefinite for the use of the term "associated with  
23 the object," should be withdrawn.

24           The Indefiniteness of the Term "If" in Claim 34

25           The Examiner further asserts that use of the qualifier "if" in steps (b) and (f) of Claim 34 is  
26 indefinite, because the preamble of the claim recites "a method for detecting a feature." The  
27 Examiner is correct with respect to the preamble of the claim, however, one of ordinary skill in the  
28 art would recognize that some features may be present in some objects, and some features may not be  
29 present in some objects. The present invention is directed to a method for detecting if a feature is  
30 associated with (or part of) an object. In the context of biological cell, features that investigators may

1 wish to detect can include cell nuclei, or specific cell proteins. Most, if not all cells will include a  
2 nuclei, however, only certain types of cells will have certain types of proteins. Thus, it is not at all  
3 inconsistent to include the qualifier “if,” because the present method is capable of not only detecting  
4 a feature that is present in a cell (or associated with an object), but the method can also determine if a  
5 particular feature is not present in a cell (or associated with an object). That is, the method detects a  
6 feature only if that feature really is associated with the object (i.e., is part of the object). Applicants  
7 could have worded the preamble to read: *A method for detecting whether or not any particular*  
8 *feature is associated with an object using an imaging system.* However, MPEP 2173.05 requires an  
9 indefinite analysis to allow some degree of latitude, and notes that any determination of whether or  
10 not a claim is indefinite must be made based on how and artisan of ordinary skill would have  
11 interpreted the claim. There does not appear to be any basis to conclude that an artisan of ordinary  
12 skill would not have understood the scope of the claim. The test is not whether applicants used the  
13 best possible language, merely whether the language employed by the applicant provides sufficient  
14 clarity and particularly such that one of ordinary skill in the art could understand the scope of the  
15 invention.

16 With respect to Claim 34, step (a) provides a labeled probe that specifically binds to a  
17 particular feature. It must be recognized that not all objects will include that particular feature. Thus,  
18 it is possible that the specific object to be imaged may not include the specific feature corresponding  
19 to the probed that is provided in step (a). In step (b), the object is exposed to the labeled probe, so  
20 that *if* the specific feature is associated with that object (i.e., if the specific feature is part of that  
21 object), the labeled probe will bind to the feature. Logically, if the specific feature is not part of that  
22 object, then no binding can occur. Artisans of ordinary skill would recognize that a probe configured  
23 to bind to a surface protein cannot bind to cells that do not include that specific protein.

24 Note that steps (d) and (e) have specifically been worded bearing in mind that for a particular  
25 object being imaged, there may or may not be features to which a labeled probe has been attached.  
26 Step (d) recites “...locations of labeled probes bound to [[a]] said feature included in the image being  
27 optically discriminated but not spatially discriminated in the image.” This recitation holds true both  
28 for objects that do not include the feature being probed, and objects including the feature being  
29 probed. If the object does not include the specific feature being probed, then the image will not  
30 include any locations of labeled probes. Step (d) does not specifically recite that the image *must*

1 include the labeled probes, just that when the image does include the labeled probes, the locations are  
2 optically discriminable, but not spatially discriminable. Step (e) recites detecting the image to  
3 produce a signal indicative of each optical signaling component bound to the feature. If no optical  
4 signaling components are bound to the feature (because the feature is not associated with or part of  
5 the object), then the signal will reflect that the feature is absent. In step (f), the signal is analyzed to  
6 determine whether or not the feature is present.

7       There appears to be no basis to conclude that one of ordinary skill in the art could not parse  
8 step (b) and understand the meaning of step (b). While the Examiner may correctly believe that  
9 applicants could have used *better* language, the proper analysis requires determining whether the  
10 language employed would have been able to be understood by an artisan of ordinary skill. The use of  
11 the term "if" in Claim 34 does not appear to render the claim indefinite with respect to the ability of  
12 an artisan of ordinary skill to read and understand the claim. Accordingly, the rejection of Claim 34  
13 under 35 U.S.C. § 112, second paragraph, as being indefinite for the use of the term "if," should be  
14 withdrawn.

15       The Indefiniteness of the Term "A Plurality of Optical Signaling Components" in Claim 34

16       The Examiner further asserts that because step (a) recites "at least one optical signaling  
17 component," step (b) is indefinite because it recites "a plurality of optical signaling components." A  
18 reasoned analysis will indicate that there is no consistency, and indeed this specific step is a key  
19 element of the multiplexing technique of the present invention. As the Examiner has noted, step (a)  
20 requires that each labeled probe includes at least one signaling component. Step (b) requires that a  
21 plurality of optical signaling components become bound to the feature. As described in detail in the  
22 specification, this can occur in at least two different ways. First, a probe including a plurality of  
23 optical signaling components can be bound to the feature. This meets the limitations recited in both  
24 steps (a) and (b). Second, two different labeled probes can be provided, each probe including an  
25 optical signaling component. As noted above, the drawings clearly indicate that some features can  
26 support more than one probe being bound to feature. Thus, two or more probes being bound to a  
27 single feature will result in a plurality of optical signaling components becoming bound to the  
28 feature. Claim 34 does not limit the invention to either possibility, but rather encompasses both  
29 possibilities identified above. As there is no inconsistency, the rejection of Claim 34 under  
30



1 35 U.S.C. § 112, second paragraph, as being indefinite for the use of the term “a plurality of optical  
2 signaling components,” should be withdrawn.

3 The Indefiniteness of the Term “A Feature” in Step (d) of Claim 34

4 The Examiner asserts that the term “a feature” in step (d) is indefinite, because it is not clear  
5 whether a feature is the same as the previously recited feature. Applicants agree, and have amended  
6 step (d) to replace “a feature” with “said feature.” As applicants have corrected this issue, the  
7 rejection of Claim 34 under 35 U.S.C. § 112, second paragraph, as being indefinite for the use of the  
8 term “a feature” in step (d), should be withdrawn.

9 The Indefiniteness of the Term “The” in Step (f) of Claim 34

10 The Examiner notes that the first occurrence of the term “the” in step (f) is a grammatical  
11 error. Applicants agree, and have amended step (f) to correct the error. As applicants have corrected  
12 this issue, the rejection of Claim 34 under 35 U.S.C. § 112, second paragraph, as being indefinite for  
13 the use of the term “the” in step (f), should be withdrawn.

14 The Indefiniteness of the Term “If” in Claims 37, 39, 41 and 42

15 The Examiner asserts that the inclusion of the qualifier “if” in Claims 37, 39, 41 and 42 is  
16 indefinite because the qualifier is not positively recited. Applicants are not aware of any statutory  
17 authority which explicitly states that the term “if” can only be used in a method step where the  
18 qualifier is positively recited. While the Examiner may believe that Claims 37, 39, 41 and 42 could  
19 have been written in a *better* format, an appropriate indefinite analysis is limited to determining  
20 whether or not an artisan of ordinary skill in the art, given the scope of the disclosure and the  
21 knowledge available in the art, would be able to understand the scope of the invention.

22 Claim 37 specifically recites “... wherein the step of analyzing the signal comprises the step  
23 of determining if an intensity of the waveband of light indicative of a plurality of optical signaling  
24 components is present in the image.” There is simply no basis for concluding that an artisan of  
25 ordinary skill would not understand the step recited in Claim 37.

26 Claim 39 specifically recites “... wherein the step of analyzing the signal comprises the step  
27 of determining if a multiplex of a spectral signal for each of the plurality of different optical signaling  
28 components is present in the image.” Given the disclosure of the specification as filed, there is  
29 simply no basis for concluding that an artisan of ordinary skill would not understand the step recited  
30 in Claim 39.

1 Claim 41 specifically recites "...the step of analyzing the signal comprises the step of  
2 analyzing each different signal produced for each of the plurality of images to determine if indicative  
3 spectral signals produced by the plurality of the optical signaling components are present in the  
4 plurality of images..." Again, there appears to be no basis for concluding that an artisan of ordinary  
5 skill would not be able to understand the scope of Claim 41.

6 With respect to Claim 42, as noted above applicants are not aware of any statutory authority  
7 that prohibits the use of the term "if" in a claim unless the term is positively recited. A proper  
8 indefinite analysis must determine whether the language employed in the claim is sufficiently clear  
9 and particular that one of ordinary skill in the art, given the scope of the disclosure and up the prior  
10 art, would understand scope of the claim. No such analysis has been provided with respect to the  
11 rejection of Claim 42 for the inclusion of the term "if."

12 Accordingly, the rejection of Claims 37, 39, 41 and 42 under 35 U.S.C. § 112, second  
13 paragraph, as being indefinite for the use of the term "if" without a positive recitation of the same,  
14 should be withdrawn.

15 The Indefiniteness of Claim 42 Because Step (d) Does Not Correlate with the Preamble

16 This issue has been addressed above with respect Claim 34. The Examiner is correct that the  
17 preamble does refer to a method to detect if a specific feature is associated with an object. Step (d)  
18 recites analyzing the signal to detect each optical signaling component bound to any specific feature  
19 associated with the object, thereby determining which specific features associated with the object.  
20 Clearly, if the signal is indicative of an optical signaling component bound to a specific feature, it  
21 then can be determined that the specific feature is associated with the object. Functionally, this  
22 enables one to detect whether or not a specific feature is associated with the object, a process that is  
23 entirely consistent with the preamble to the claim. In answer to the Examiner's question of whether a  
24 feature should be detected, a feature will be detected if that feature is associated with the object, and  
25 if a labeled probe has been attached to the feature. It is entirely possible that the feature in question  
26 (for example, a specific surface protein) may not be present, and thus in some cases no feature would  
27 be detected.

28 The Examiner's position is not entirely clear, but it may be that the Examiner has rejected  
29 Claim 42 simply because the preamble states "A method for probing an object to detect if any of a  
30 plurality of specific features is associated with the object...", whereas an entirely parallel recitation is

1 not present in step (d). Regardless of the fact that step (d) does not include a parallel recitation, in  
2 practical terms implementing step (d) functionally results in detecting if any of a plurality of specific  
3 features are associated with the object. This result is achieved by analyzing the signal, to determine if  
4 the signal is indicative of the signaling component bound to a specific feature. If an indication of a  
5 specific signaling component is present in the signal, logically it can be concluded that the specific  
6 feature corresponding to that specific signaling component is present. Similarly, if no indication of a  
7 specific signaling component is present in the signal, logically it can be concluded that the specific  
8 feature corresponding to that specific signaling component is not present. Thus, implementing  
9 steps (a)-(d) probes an object to detect if any of the plurality of specific features are associated with  
10 the object.

11 There is no statutory requirement for a parallel recitation, such that the final step of the  
12 method claim *exactly* mirrors the language used in the preamble. Clearly, the method steps recited  
13 enable the detection referred to in the preamble to be achieved. There simply is no basis to conclude  
14 that one of ordinary skill in the art would not understand that implementing steps (a)-(d) enable an  
15 object to be probed to detect if any of a plurality of specific features are associated with the object.  
16 Accordingly, the rejection of Claim 42 under 35 U.S.C. § 112, second paragraph, as being indefinite  
17 because step (d) does not correlate with the preamble of the claim, should be withdrawn.

18 The Indefiniteness of the Term "Sufficient" in Claim 49

19 The Examiner asserts that Claim 49 is indefinite because the term "sufficient" is a relative  
20 term that lacks a comparative basis for defining its meets and bounds. Claim 49 specifically recites  
21 "...directing sufficient energy towards said object, such that the fluorescent dye is excited to emit  
22 fluorescent light..." There appears to be no indefiniteness here. *Any* quantity of energy which causes  
23 a fluorescent emission is sufficient energy. *Any* quantity of energy which does not cause a  
24 fluorescent emission is not sufficient. One of ordinary skill in the art would readily recognize that  
25 different fluorophores are stimulated using different energy levels. The determination of exactly  
26 what energy level is required to cause a specific fluorescent dye to emit light is well within the realm  
27 of that which an artisan of ordinary skill can accomplish with out requiring detailed instructions.  
28 Fluorescent dyes in general are very well researched, thus a large body of data can be consulted to  
29 determine energy levels required to cause a specific fluorescent dye to emit light. Furthermore, a  
30 very simple empirical experiment can be performed to determine whether a given energy level is

1 sufficient, or not sufficient. There is no evidence that such a determination would require undue  
2 experimentation. It is a well accepted principle in patent prosecution that *that which is known* need  
3 not be described in detail, and determining what quantity of energy is sufficient is clearly well within  
4 the skill of the ordinary artisan. Accordingly, the rejection of Claim 49 under 35 U.S.C. § 112,  
5 second paragraph, as being indefinite for the use of the term “sufficient,” should be withdrawn.

6 The Indefiniteness of the Term “Spectral Composition of Light” in Claim 51

7 The Examiner has requested clarification of the term “spectral composition of light” as  
8 utilized in Claim 51. This concept is schematically illustrated in FIGURE 11, which shows a single  
9 cell labeled with a single multiplexed FISH probe having two FISH emission spectra. That is, a  
10 feature in cell 150 of FIGURE 11 is labeled with a probe that includes two different optical signaling  
11 elements, where each optical signaling element has a different spectral signal. Assume the two  
12 optical signaling elements comprise a red fluorescent dye and a green fluorescent dye. Thus, in a  
13 spectrally dispersed image, the feature will appear twice, once as a red image and once as a green  
14 image. Now consider a different feature that is labeled with a probe which also includes two  
15 different optical signaling elements, but this time the optical signaling elements comprise a red  
16 fluorescent dye and a yellow fluorescent dye. In a spectrally dispersed image, the feature will appear  
17 twice, once as a red image and once as a yellow image. The two features can be identified based on  
18 the spectrally dispersed image. The first feature is uniquely discriminable based on its spectral  
19 composition of light; a spectrally dispersed image of the first feature will include both a red image  
20 and a green image. The second feature is also uniquely discriminable based on its spectral  
21 composition of light; a spectrally dispersed image of the second feature will include both a red image  
22 and a yellow image. This process is explained in detail in the specification as filed, particularly with  
23 respect to FIGURES 2A-2G and FIGURE 3.

24 Applicants respectfully submit that given the disclosure provided in the application as filed,  
25 an artisan of ordinary skill would be able to understand the scope of Claim 51. Accordingly, the  
26 rejection of Claim 51 under 35 U.S.C. § 112, second paragraph, as being indefinite for the use of the  
27 term “spectral composition of light,” should be withdrawn.

1 Rejection of Claims under 35 U.S.C. § 102

2 The Examiner has rejected Claims 34-51 under 35 U.S.C. § 102 as being anticipated by  
3 Dunlay (U.S. Patent No. 6,620,591). The Examiner asserts that Dunlay discloses each element of  
4 applicants' claimed invention. Applicants respectfully disagree for the following reasons.

5 The present invention can be distinguished from Dunlay for at least two reasons. First, at  
6 least some of the labeled probes employed in the present invention to uniquely identify a specific  
7 feature of an object include more than one type of signaling component. The prior art uses only one  
8 type of signaling component for each feature to be probed. For example, Dunlay describes using up  
9 to four different colors, which enables four different features to be probed at one time. The  
10 significance of the present invention is that at least one feature associated with an object will be  
11 probed using at least two different signaling components. This is what applicants have intended to  
12 convey by using the term multiplexing in the specification. By using more than one type of signaling  
13 component for a specific feature to be probed, a relatively small set of signaling components can be  
14 used to uniquely identify a relatively large number of different features. This concept is clearly  
15 described in the specification as filed, particularly with respect to FIGURE 1. A relatively simple  
16 embodiment of this concept is clearly described in conjunction with FIGURE 2B. Feature 1 of  
17 FIGURE 2B is uniquely identified by signaling element 410a. Feature 2 is uniquely identified by  
18 signaling element 410b. Significantly, Feature 3 is uniquely identified by detecting the presence of  
19 both signaling element 410a and signaling element 410b on the same feature. Thus two different  
20 signaling elements can uniquely identify three different features. The cited art simply does not teach  
21 or suggest identifying a specific feature by using more than one type of signaling element for one  
22 specific feature.

23 Claim 34 has been amended to make this distinction clear. Claims 35-38 and 40 have been  
24 amended so that the dependent claims are consistent with Claim 34 as amended. There is no  
25 evidence that one of ordinary skill in the art would have modified the technique disclosed by Dunlay,  
26 or any other prior art, to achieve an equivalent invention. Each claim depending upon Claim 34 must  
27 be patentable for at least the same reasons. Accordingly, the rejection of Claims 34-41 as a being  
28 anticipated by Dunlay should be withdrawn.

29 The present invention can also be distinguished over Dunlay because in the present invention  
30 data from all probes bound to a specific feature of an object are collected *simultaneously*. According

1 to Dunlay, data for each channel must be collected individually. Dunlay clearly describes that  
2 initially data for a primary channel is collected, and that collected data is processed (see step 105 of  
3 FIGURE 7, and column 6, lines 33 to 43). Only later will data for each additional channel be  
4 collected. When four different fluorescent labels are used, four channels of data are collected. Note  
5 Dunlay explicitly teaches that the cameras exposure time is *separately adjusted* for each dye to  
6 ensure a high quality image from each channel (column 6, lines 32-35). Logically, the only way the  
7 camera can be separately adjusted for each channel is if data for each channel is collected at a  
8 different time.

9 Step (c) of Claim 42 explicitly recites the step of "simultaneously detecting light from all  
10 optical signaling components associated with the object," in distinct contrast to Dunlay's technique of  
11 collecting light for each different dye separately. The techniques simply are not equivalent. It is well  
12 understood that dependent claims must be patentable for at least the same reasons as claims upon  
13 which they depend, thus, each claim depending from Claim 42 must also be patentable

14 There is no basis for concluding that it would have been obvious to one of ordinary skill in the  
15 art to modify Dunlay's technique to achieve applicants' invention as defined in Claim 42.  
16 Accordingly, the rejection of Claims 42-51 as a being anticipated by Dunlay, should be withdrawn.

17 Further, Claim 45 specifically recites a labeled probe the comprises at least two different  
18 optical signaling components. As discussed in detail above, Dunlay does not teach or suggest this  
19 concept. Claim 45 is therefore distinguishable over the cited art for this additional reason.

#### 20 Patentability of Newly Added Claims

21 Applicants have added new claims 52 and 53, neither of which introduces new matter.

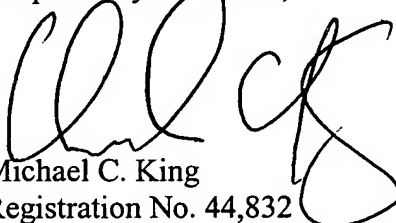
22 Claim 52 employs the term "physical feature" in place of the term "feature." As discussed  
23 above, it does not appear reasonable to conclude that one of ordinary skill in the art would not  
24 understand the term feature as employed in the original claims. However, in the interest of advancing  
25 prosecution in the present application, applicants have incorporated the term physical feature in the  
26 newly added claims. Claim 52 represents a redrafting of Claim 34 to emphasize the novel aspects of  
27 the present invention. Significantly, Claim 52 recites both the element of using at least two different  
28 spectrally distinguishable optical signaling components to uniquely identify a specific physical  
29 feature, and simultaneously collecting light from all optical signaling components associated with an  
30 object. As discussed above, Dunley specifically describes collecting light from the different

1 fluorescent dyes separately, and using only one signaling element (i.e., fluorescent dye) to uniquely  
2 identify each feature. Claim 52 is therefore patentable in view of the cited art.

3 Claim 53 is generally based on Claim 42, and defines a process for probing an object to  
4 determine if any one of a plurality of different physical features are associated with that object.  
5 Significantly, labeled probes configured to selectively bind to at least one specific physical feature  
6 include at least two different types of signaling components that can be spectrally distinguished. As  
7 described in detail in the specification is filed, this can be achieved by having each individual probe  
8 in a set of labeled probes include two different optical signaling elements (see the probe bound to  
9 Feature 3 of FIGURE 2B), or the set of labeled probes configured to selectively bind it to a specific  
10 physical feature can include some labeled probes including a first optical signaling element and some  
11 labeled probes including a different optical signaling element (see the set of labeled probes bound to  
12 Feature 3 of FIGURE 2D). The cited art does not teach or suggest uniquely identifying a specific  
13 physical feature using more than one signaling component. Claim 53 also recites that light from all  
14 optical signaling components associated with an object are collected simultaneously. Dunley  
15 specifically describes collecting light from the different fluorescent dyes separately. Thus, Claim 53  
16 is distinguishable over the cited art.

17 Accordingly, all of the claims now submitted define patentable subject matter that is neither  
18 anticipated nor obvious in view of the prior art cited. The Examiner is thus requested to issue the  
19 present patent in view of the amendments and the remarks submitted above. If there are any  
20 questions that might be addressed by a telephone interview, the Examiner is invited to telephone the  
21 undersigned attorney, at the number listed below.

22 Respectfully submitted,

23   
24 Michael C. King  
25 Registration No. 44,832  
26

27 MAILING CERTIFICATE

28 I hereby certify that this correspondence is being deposited with the U.S. Postal Service in a sealed  
29 envelope as first class mail with postage thereon fully prepaid addressed to: Commissioner for Patents,  
30 Alexandria, VA 22313-1450, on May 12, 2005.

Date: May 12, 2005

